



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : Cederberg et al.
Serial No. : 08/945,425
Filed : October 21, 1997
For : ADMINISTRATION OF
PHARMACEUTICALS
Examiner : R. Desai
Group Art Unit : 1612

TECH CENTER 1600/2900

JUL 31 2001

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DECLARATION OF CHRISTER CEDERBERG
(Under 37 C.F.R. § 1.132)

Sir:

I, Christer Cederberg, Ph.D., declare as follows:

1. I am a citizen of SWEDEN. I graduated in 1992 from the University of Gothenburg, Sweden, Department of Clinical Pharmacology, with a doctorate in Medical Science.
2. AstraZeneca is the assignee of the referenced application. AstraZeneca R&D Boston, Cambridge has employed me from 1999 to the present as the Director of Clinical Pharmacology and Animal Science. From 1979 to 1999, I was employed in various positions at AB Hässle and Astra Hässle AB which are also presently part of the AstraZeneca organization. I have read and understood the referenced patent application. As a named inventor, I am familiar with the invention described and claimed in the referenced application. My curriculum vitae is enclosed (Exhibit A).

3. Set forth below is a summary of a clinical study performed by Astra Hässle AB on pharmaceutical formulations of omeprazole having the chemical name, 5-methoxy-2-(((4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl) sulfinyl)-1H-benzimidazole. As used herein, omeprazole refers to the racemic form of omeprazole.
4. The study concerns a clinical comparison of the pharmacokinetics of a multiple unit dosage form (capsule) comprising the non-salt form of omeprazole and a multiple unit tableted dosage form comprising the magnesium salt of omeprazole. The results demonstrate that the respective formulation of the capsule comprising the non-salt form of omeprazole and the multiple unit tablet comprising the magnesium salt of omeprazole are bioequivalent.
5. As described in the Example at pages 10-11 of the subject application, the pharmacological effect of the claimed method of treatment was compared with a conventional administration regimen involving omeprazole racemate. Specifically, omeprazole racemate was administered in the form of Prilosec® omeprazole capsules. A first group of subjects received Prilosec® 20 mg twice daily with 3 hours apart from administration. A second group of subjects received a single daily dose of Prilosec® 40. With each group of subjects, the efficacy of the respective administration regimen in controlling acid secretion was measured. The results showed that the therapeutic effect of omeprazole is maximized when the blood plasma concentration of the drug is extended by repeated single doses of omeprazole which are administered with 3 hours apart from each administration, when compared to a single dose. The expression "blood plasma profile" as used herein and throughout the specification of the subject application and as understood by the person of ordinary skill in the art, means the measurable concentration of the drug, i.e., the H⁺,K⁺-ATPase inhibitor, e.g., omeprazole, at any time subsequent to administration.
6. Applicants were requested by the Examiner during the Interview of April 10, 2001 to repeat the Example of the subject application with the multiple unit dosage form of U.S. Patent No. 5,753,265 (the "265 patent"). The '265 patent is a cited prior art reference. A commercial product in accordance with the '265 patent is Losec® MUPS® tablets containing omeprazole magnesium salt as the active ingredient. Losec® MUPS® tablets are not currently sold in the United States. The following clinical study demonstrates that Prilosec® omeprazole capsules, i.e.,

the dosage form administered in the Example of the subject application, and Losec® MUPS® tablets of the cited '265 patent, are bioequivalent.

Clinical Study

A comparative study involving the absorption of omeprazole from separate formulations: Prilosec®, i.e., the non-salt form of omeprazole, and Losec® MUPS®, the magnesium salt of omeprazole.

The clinical study is an open, randomized, two-way cross-over trial consisting of two study periods. Each study period consisted of six days of daily oral administration of 20 mg of omeprazole or omeprazole-Mg. The pharmacokinetics (plasma levels) of the compound was studied on day 1 and day 6. Twenty-eight Caucasian subjects were included and completed the study.

Table 1: Area under the plasma concentration versus time curve (AUC; $\mu\text{mol} \times \text{h/L}$) after oral administration of 20 mg of omeprazole and omeprazole-Mg, respectively.

	Day 1		Day 6	
	Omeprazole	Omeprazole-Mg	Omeprazole	Omeprazole-Mg
Geometric mean	0.84	0.86	1.48	1.56
95% Confidence interval	0.66-1.10	0.66-1.12	1.11-1.96	1.14-2.12
Coefficient of variation (%)	82.5	72.6	80.5	93.6

The results from the clinical study indicate that the same amount of substance is absorbed irrespective of the formulation administered, i.e., the non-salt form of omeprazole racemate or the Mg-salt of omeprazole racemate. Therefore, these formulations can be considered to be "bioequivalent". Furthermore, the interindividual variation, calculated as the coefficient of variation for the two formulations, is comparable.

Conclusions

The clinical study outlined above shows that Prilosec® omeprazole capsules, i.e., the dosage form administered in the Example of the subject application, and Losec® MUPS® tablets of the cited '265 patent are bioequivalent. Therefore, the unexpected advantages described in the Example of the subject application would have been obtained with Losec® MUPS® tablets of the cited '265 patent when administered twice daily with 3 hours apart, when compared to a single dose (40 mg). Accordingly, the clinical study outlined above and conclusions are fully responsive to the Examiner's request for a side-by-side comparison with the tablet dosage form of the '265 patent.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated:

Christer Cederberg, Ph.D.

CURRICULUM VITAE

Family name: Cederberg
 Given name: Hans Christer
 Date of birth: 18 april 1951
 Citizenship: Swedish

Education:	1975	B.Sc in Biology and Chemistry
	1975-79	Research student at Department of Zoophysiology, University of Gothenburg, Sweden
	1992	Doctor in Medical Science (Ph.D), Dept of Clinical Pharmacology, University of Gothenburg, Sweden
Previous positions:	1976-78	Assistant Teacher, Dept of Zoophysiology, University of Gothenburg, Sweden
	1979-81	Clinical Research Monitor, Medical Department, AB Hässle, Mölndal, Sweden
	1981-82	Clinical Research Coordinator, Medical Department , AB Hässle, Mölndal, Sweden
	1982-86	Clinical Research Manager, Medical Department, AB Hässle, Mölndal, Sweden
	1986-90	Associate Director, Gastrointestinal Clinical Pharmacology and Medicine, AB Hässle, Mölndal, Sweden
	1991-94	Associate Director, Clinical Pharmacology, Astra Hässle AB, Mölndal, Sweden
	1994-98	Scientific Adviser, Astra Hässle AB, Mölndal, Sweden
	1994-98	Project Director, Helicobacter pylori Clinical Research, Astra Hässle AB, Mölndal, Sweden
	1996-98	Member of Losec Board, Astra Hässle AB, Mölndal, Sweden
	1996-98	Chairman of Losec Working Party, Astra Hässle AB, Mölndal, Sweden
	1998-99	Director Clinical Pharmacology, Astra Research Center Boston, Cambridge, USA

Present position

1999- Director Clinical Pharmacology and Animal Science, AstraZeneca R&D Boston, Cambridge, USA

Membership:

Nordic Association for Physiology

European Association for Gastroenterology & Endoscopy

The British Society of Gastroenterology

Invited speaker to international symposia

Scandinavian workshop on regulatory mechanisms in gastric secretion - differences between animals, normal individuals and duodenal ulcer patients and implications on peptic ulcer research. Nyborg, Denmark, 18-19 august, 1981

The international Symposium on Omeprazole, Monte-Carlo, 11-12 November, 1988

Focus on gastric pump inhibitors: An update on treatment decisions in peptic ulcer disease. Toronto, Ontario, Canada 12 May, 1989

Conference on Gastrin, Dana Point, California, USA, 9-12 February 1992

Landmarks and future development in the era of acid pump inhibitors. Sidney, Australia, July, 1996

Second European Congress of Chemotherapy and 7th biannual Conference on Antiinfective Agents and Chemotherapy, Hamburg, Germany, 10-13 May, 1998

Publications:

1. Holstein B, Cederberg C. Effect of vagotomy and glucose administration on gastric acid secretion in the Atlantic cod, *Gadus morhua*. *Acta Physiologica Scandinavica* 1980;109(1):37-44.

2. Frech W, Cedergren A, Cederberg C, Vessman J. Evaluation of some critical factors affecting determination of aluminum in blood, plasma, or serum by electrothermal atomic absorption spectroscopy. *Clinical Chemistry* 1982;28(11):2259-63.

3. Olbe L, Haglund U, Leth R, Lind T, Cederberg C, Ekenved G, Elander B, Fellenius E, Lundborg P, Wallmark B. Effects of substituted benzimidazole (H 149/94) on gastric acid secretion in humans. *Gastroenterology* 1982;83:193-8.
4. Lind T, Cederberg C, Ekenved G, Haglund U, Olbe L. Effect of omeprazole--a gastric proton pump inhibitor--on pentagastrin stimulated acid secretion in man. *Gut* 1983;24(4):270-6.
5. Londong W, Londong V, Cederberg C, Steffen H. Dose-response study of omeprazole on meal-stimulated gastric acid secretion and gastrin release. *Gastroenterology* 1983;85(6):1373-8.
6. Holstein B, Cederberg C. Effect of 5-HT on basal and stimulated secretions of acid and pepsin and on gastric volume outflow in the in vivo gastrically and intestinally perfused cod, *Gadus morhua*. *Agents & Actions* 1984;15(3-4):291-305.
7. Olbe L, Lind T, Carlsson E, Cederberg C, Helander H, Wallmark B, Larsson H. [Pharmacological background for therapeutic use of a proton pump inhibitor]. [French]. *Méd et Hyg* 1984;42:274-8.
8. Olbe L, Lind T, Carlsson E, Cederberg C, Helander H, Wallmark B. [Acid secretion inhibition with new mechanisms of action: substituted benzimidazole]. [German]. *Schweizerische Medizinische Wochenschrift* 1984;114:683-5.
9. Cederberg C, Ekenved G, Lind T, Olbe L. Acid inhibitory characteristics of omeprazole in man. *Scandinavian Journal of Gastroenterology - Supplement* 1985;108:105-12.
10. Pilbrant A, Cederberg C. Development of an oral formulation of omeprazole. *Scandinavian Journal of Gastroenterology - Supplement* 1985;108:113-20.
11. Holstein B, Cederberg C. Effects of tachykinins on gastric acid and pepsin secretion and on gastric outflow in the Atlantic cod, *Gadus morhua*. *American Journal of Physiology* 1986;250(3:Pt 1):Pt 1:G309-15.
12. Lind T, Cederberg C, Ekenved G, Olbe L. Inhibition of basal and betazole- and sham-feeding-induced acid secretion by omeprazole in man. *Scandinavian Journal of Gastroenterology* 1986;21(8):1004-10.
13. Olbe L, Lind T, Cederberg C, Ekenved G. Effect of omeprazole on gastric acid secretion in man. *Scandinavian Journal of Gastroenterology - Supplement* 1986;118:105-7.
14. Lanzon-Miller S, Pounder RE, Hamilton MR, Chronos NA, Ball S, Mercieca JE, Olausson M, Cederberg C. Twenty-four-hour intragastric acidity and plasma gastrin concentration in healthy subjects and patients with duodenal or gastric ulcer, or pernicious anaemia. *Alimentary Pharmacology & Therapeutics* 1987;1(3):225-37.

15. Lanzon-Miller S, Pounder RE, Hamilton MR, Ball S, Chronos NA, Raymond F, Olausson M, Cederberg C. Twenty-four-hour intragastric acidity and plasma gastrin concentration before and during treatment with either ranitidine or omeprazole. *Alimentary Pharmacology & Therapeutics* 1987;1(3):239-51.
16. Sharma B, Axelson M, Pounder RP, Lundborg P, Ohman M, Santana A, Talbot M, Cederberg C. Acid secretory capacity and plasma gastrin concentration after administration of omeprazole to normal subjects. *Alimentary Pharmacology & Therapeutics* 1987;1(1):67-76.
17. Holstein B, Cederberg C. Effect of somatostatin on basal and stimulated gastric secretion in the cod, *Gadus morhua*. *American Journal of Physiology* 1988;254(2:Pt 1):Pt 1):G183-8.
18. Lind T, Cederberg C, Forssell H, Olausson M, Olbe L. Relationship between reduction of gastric acid secretion and plasma gastrin concentration during omeprazole treatment. *Scandinavian Journal of Gastroenterology* 1988;23(10):1259-66.
19. Cederberg C. Pharmacology of proton pump inhibitors in man. *Can J Gastroenterol* 1989;3(Suppl A):43-8.
20. Cederberg C, Andersson T, Skanberg I. Omeprazole: pharmacokinetics and metabolism in man. [Review] [23 refs]. *Scandinavian Journal of Gastroenterology - Supplement* 1989;166:33-40.
21. Olbe L, Cederberg C, Lind T, Olausson M. Effect of omeprazole on gastric acid secretion and plasma gastrin in man. *Scandinavian Journal of Gastroenterology - Supplement Vol 24(166)* (pp 27-32), 1989;
22. Olbe L, Cederberg C, Lind T, Olausson M. Effect of omeprazole on gastric acid secretion and plasma gastrin. [Review] [23 refs]. *Journal of Gastroenterology & Hepatology* 1989;4:Suppl 2:19-25.
23. Andersson T, Andren K, Cederberg C, Heggelund A, Lundborg P, Rohss K. Bioavailability of omeprazole as enteric coated (EC) granules in conjunction with food on the first and seventh days of treatment. *Drug Investigation* 1990;2(3):184-8.
24. Andersson T, Cederberg C, Edvardsson G, Heggelund A, Lundborg P. Effect of omeprazole treatment on diazepam plasma levels in slow versus normal rapid metabolizers of omeprazole. *Clinical Pharmacology & Therapeutics* 1990;47(1):79-85.
25. Andersson T, Andren K, Cederberg C, Edvardsson G, Heggelund A, Lundborg P. Effect of omeprazole and cimetidine on plasma diazepam levels. *European Journal of Clinical Pharmacology* 1990;39(1):51-4.
26. Andersson T, Cederberg C, Regardh CG, Skanberg I. Pharmacokinetics of various single intravenous and oral doses of omeprazole. *European Journal of Clinical Pharmacology* 1990;39(2):195-7.

27. Andersson T, Andren K, Cederberg C, Lagerstrom PO, Lundborg P, Skanberg I. Pharmacokinetics and bioavailability of omeprazole after single and repeated oral administration in healthy subjects. *British Journal of Clinical Pharmacology* 1990;29(5):557-63.
28. Lind T, Cederberg C, Olausson M, Olbe L. 24-hour intragastric acidity and plasma gastrin after omeprazole treatment and after proximal gastric vagotomy in duodenal ulcer patients [see comments]. *Gastroenterology* 1990;99(6):1593-8.
29. Vinayek R, Frucht H, London JF, Miller LS, Stark HA, Norton JA, Cederberg C, Jensen RT, Gardner JD, Maton PN. Intravenous omeprazole in patients with Zollinger-Ellison syndrome undergoing surgery [published erratum appears in *Gastroenterology* 1990 Sep;99(3):905]. *Gastroenterology* 1990;99(1):10-6.
30. Andersson T, Bergstrand R, Cederberg C, Eriksson S, Lagerstrom PO, Skanberg I. Omeprazole treatment does not affect the metabolism of caffeine. *Gastroenterology* 1991;101(4):943-7.
31. Andersson T, Cederberg C, Heggelund A, Lundborg P. The pharmacokinetics of single and repeated once-daily doses of 10, 20 and 40mg omeprazole as enteric-coated granules. *Drug Investigation* 1991;3(1):45-52.
32. Andersson T, Bergstrand R, Cederberg C. Influence of acid secretory status on absorption of omeprazole from enteric coated granules. *British Journal of Clinical Pharmacology* 1991;31(3):275-8.
33. Lind T, Cederberg C, Olausson M, Olbe L. Omeprazole in elderly duodenal ulcer patients: relationship between reduction in gastric acid secretion and fasting plasma gastrin. *European Journal of Clinical Pharmacology* 1991;40(6):557-60.
34. Lind T, Cederberg C, Idstrom J, Lonroth H, Olbe L, Lundell L. 24-hour intragastric acidity and plasma gastrin during long-term treatment with omeprazole or ranitidine in patients with reflux esophagitis. *Scandinavian Journal of Gastroenterology* 1991;26(6):620-6.
35. Cederberg C, Rohss K, Lundborg P, et al. Cederberg C, editors. Clinical pharmacology of intravenous omeprazole; Experimental studies in healthy subjects and duodenal ulcer patients. 1992; I, Effect of intravenous omeprazole on pentagastrin stimulated acid secretion in healthy subjects. p. 1-20.
36. Cederberg, C. Clinical pharmacology of intravenous omeprazole; Experimental studies in healthy subjects and duodenal ulcer patients 1992; Dept of Clinical Pharmacology, University of Gothenburg; 1 p.
37. Cederberg C, Lind T, Rohss K, Olbe L. Comparison of once-daily intravenous and oral omeprazole on pentagastrin-stimulated acid secretion in duodenal ulcer patients. *Digestion* 1992;53(3-4):171-8.

38. Cederberg C, Thomson ABR, Mahachai V, Westin JA, Kirdeikis P, Fisher D, Zuk L, Marriage B. Effect of intravenous and oral omeprazole on 24-hour intragastric acidity in duodenal ulcer patients. *Gastroenterology* 1992;103(3):913-8.
39. Cederberg C, Bergstrand R, Lundborg P, et al. Cederberg C, editors. Clinical pharmacology of intravenous omeprazole; Experimental studies in healthy subjects and duodenal ulcer patients. 1992; V, Intragastric acidity during intravenous infusion of omeprazole. p. 1-19.
40. Cederberg C, Rohss K, Lundborg P, Olbe L. Effect of once daily intravenous and oral omeprazole on 24-hour intragastric acidity in healthy subjects. *Scandinavian Journal of Gastroenterology* 1993;28(2):179-84.
41. Verdu E, Viani F, Armstrong D, Fraser R, Siegrist HH, Pignatelli B, Idstrom J, Cederberg C, Blum AL, Fried M. Effect of omeprazole on intragastric bacterial counts, nitrates, nitrites, and N-nitroso compounds. *Gut* 1994;35(4):455-60.
42. Hunt RH, Cederberg C, Dent J, Halter F, Howden C, Marks IN, Rune S, Walt RP. Optimizing acid suppression for treatment of acid-related diseases. [Review] [292 refs]. *Digestive Diseases & Sciences* 1995;40(2:Suppl):Suppl):24S-49S.
43. Verdu EF, Armstrong D, Fraser R, Viani F, Idstrom J, Cederberg C, Blum AL. Effect of *Helicobacter pylori* status on intragastric pH during treatment with omeprazole. *Gut* 1995;36(4):539-43.
44. Goddard AF, Jessa MJ, Barrett DA, Shaw PN, Idstrom J, Cederberg C, Spiller RC. Effect of omeprazole on the distribution of metronidazole, amoxicillin, and clarithromycin in human gastric juice [see comments]. *Gastroenterology* 1996;111(2):358-67.
45. Lind T, Veldhuyzen van Zanten SJO, Unge P, Spiller RC, Bayerdörffer E, OMorain C, Bardhan KD, Bradette M, Chiba N, Wrangstadh M, Cederberg C, Idstrom J. Eradication of *Helicobacter pylori* using one-week triple therapies combining omeprazole with two antimicrobials: The MACH 1 study. *Helicobacter* 1996;1:138-44.
46. Bercik P, Verdu EF, Armstrong D, Idstrom J, Cederberg C, Markert M, Crabtree JE, Stolte M, Blum AL. The role of ammonia and other neutralizing substances in gastric juice in subjects with *Helicobacter pylori* infection. *Gastroenterology* 1998;Submitted
47. Lind T, Megraud F, Unge P, Bayerdörffer E, OMorain C, Veldhuyzen van Zanten SJO, Wrangstadh M, Zeijlon L, Cederberg C. The MACH 2 study - The role of omeprazole in eradication of *Helicobacter pylori* with one-week triple therapies - A randomised double-blind study. *Gastroenterology* 1998;Submitted
48. Viani F, Verdu EF, Idstrom J, Cederberg C, Fraser R, Blum AL, Armstrong D. The effect of omeprazole on regional and temporal variations in intragastric acidity. *Gastroenterology* 1998;Submitted

Abstracts

1. Ekenved G, Carlsson E, Cederberg C, et al. Studies with H168/68, a novel gastric acid secretion inhibitor. [Abstract] *Gut* 1981;22:A877
2. Lind T, Olbe L, Cederberg C, et al. Effect of a substituted benzimidazole H 149/94 on gastric acid secretion in man. [Abstract] *Scand J Gastroenterol* 1981;16:1103 (Abstract 42)
3. Lind T, Cederberg C, Ekenved G, et al. [Effect of substituted benzimidazoles on acid secretion in man]. [Swedish]. [Abstract] *Acta Societatis* 1981;90:(5)152
4. Olbe L, Haglund U, Lind T, et al. Inhibition of gastric acid secretion by substituted benzimidazoles. [Abstract] *Hepatogastroenterology* 1981;29:88
5. Lind T, Cederberg C, Ekenved G, et al. The duration of the inhibitory effect of omeprazole on gastric acid secretion in healthy subjects. [Abstract] *Scandinavian Journal of Gastroenterology* 1982;17:(Supplement 78)14
6. Lind T, Cederberg C, Ekenved G, et al. Effect of single doses of omeprazole on basal and stimulated acid secretion in man. [Abstract] *Scand J Gastroenterol* 1983;(Supplement 86)45
7. Londong W, Londong V, Cederberg C, et al. Dose-response study of omeprazole on meal-stimulated gastric acid secretion and gastrin release in man. [Abstract] *Australian & New Zealand Journal of Medicine* 1983;13:326
8. Cederberg C, Lind T, Axelson M, et al. Long-term acid inhibitory effect of different daily doses of omeprazole 24 hours after dosing. [Abstract] *Gastroenterology* 1984;86:(5 part 2)1043
9. Holstein B, Cederberg C. Substance P and related tachykinins stimulate pepsin secretion in the codfish *Gadus morhua*. [Abstract] *Digestive Diseases & Sciences* 1984;29:(8 suppl)38S
10. Sharma B, Lundborg P, Pounder RE, et al. Acid secretory capacity after treatment with omeprazole. [Abstract] *Gut* 1984;25:(10)A1181
11. Cederberg C, Lind T, Olbe L. Effect of omeprazole on basal and stimulated acid secretion in man. [Abstract] *Clinical and Investigative Medicine* 1985;8:(3)C335
12. Olbe L, Carlsson E, Cederberg C, et al. Effect of H⁺K⁺-ATPase inhibitors on gastric acid secretion and ulcer healing. [Abstract] *Digestion* 1985;31:144-5.
13. Cederberg C, Andersson T, Skanberg I. Omeprazole; pharmacokinetics and metabolism in man. [Abstract] *Scandinavian Journal of Gastroenterology* 1986;(Suppl 118)

14. Lind T, Cederberg C, Axelson M, et al. Long term acid inhibitory effect of different daily doses of omeprazole 24 hours after dosing. [Abstract] Scandinavian Journal of Gastroenterology 1986;(Suppl 118)137-8.
15. Sharma B, Lundborg P, Pounder RE. Acid secretory capacity after treatment with omeprazole. [Abstract] Scandinavian Journal of Gastroenterology 1986;(Suppl 118)143-4.
16. Lanzon-Miller S, Pounder RE, Hamilton MR, et al. 24-hour intragastric acidity and plasma gastrin concentration in patients with duodenal ulcer, gastric ulcer or pernicious anemia and healthy volunteers. [Abstract] Gastroenterology 1987;95:(5 part 2)1492
17. Lind T, Cederberg C, Olausson M, et al. 24-hour intragastric acidity and plasma gastrin after omeprazole treatment or proximal gastric vagotomy in duodenal ulcer patients. [Abstract] Gastroenterology 1988;94:A265
18. Lind T, Cederberg C, Olausson M, et al. 24-hour intragastric acidity and plasma gastrin after omeprazole (OME) treatment or proximal gastric vagotomy (PGV) in duodenal ulcer (DU) patients. [Abstract] Gastroenterology International 1988;1:(Suppl 1)Abstract 724
19. Olbe L, Cederberg C, Lind T, et al. Effect of omeprazole on gastric acid secretion and plasma gastrin in man. [Abstract] Scand J Gastroenterol 1988;(Suppl 118)
20. Andersson T, Cederberg C, Heggelund A, et al. Omeprazole pharmacokinetics of single and repeated once daily administration of 10, 20, and 40 mg as enteric coated granules. [Abstract] Eur J Clin Pharmacol 1989;36:(Suppl)A142
21. Lind T, Cederberg C, Olausson M, et al. 24-hour intragastric acidity and plasma gastrin after omeprazole treatment or proximal gastric vagotomy in duodenal ulcer patients. [Abstract] Scand J Gastroenterol 1989;160:(Suppl 166)160
22. Thomson ABR, Mahachai V, Westin JA, et al. Comparison between the effect of intravenous and oral omeprazole on 24-hour intragastric acidity in duodenal ulcer patients in remission. [Abstract] Clin Invest Med 1989;12:(Suppl 4)B42
23. Cederberg C, Bergstrand R. Continuous iv-infusion of omeprazole effectively controls intragastric pH even during pentagastrin challenge. [Abstract] Gastroenterology 1990;98:(5 Part 2)A29
24. Cederberg C, Bergstrand R. Continuous iv-infusion of omeprazole effectively controls intragastric pH even during pentagastrin challenge. [Abstract] World Congress of Gastroenterology, Sidney 1990;Abstract p1030:
25. Lind T, Cederberg C, Idstrom J, et al. Twenty-four-hour intragastric acidity and plasma gastrin during short- and long-term treatment with omeprazole or ranitidine. [Abstract] European Journal Gastroenterology Hepatology 1990;2:(Suppl 1)S59-60.

26. Lind T, Cederberg C, Idstrom J, et al. 24-hour intragastric acidity and plasma gastrin during short-term and long-term treatment with omeprazole or ranitidine. [Abstract] *Scand J Gastroenterol* 1990;176:A79
27. Lind T, Cederberg C, Idstrom J, et al. 24-hour intragastric acidity and plasma gastrin during short-term and long-term treatment with omeprazole or ranitidine. [Abstract] *Gastroenterology* 1990;98:(5 Part 2)A79
28. Olbe L, Lind T, Cederberg C. Experimental and clinical pharmacology of omeprazole. [Abstract] *Digestive Diseases & Sciences* 1990;35:(8)1038
29. Rohss K, Bergstrand R, Cederberg C, et al. Effect of intravenous omeprazole on basal and stimulated cortisol and 11-deoxycortisol levels in healthy subjects. [Abstract] *Gastroenterology* 1990;98:(5 Part 2)A114
30. Thomson ABR, Mahachai V, Westin JA, et al. Comparison between the effects of intravenous and oral omeprazole on 24 h intragastric acidity. [Abstract] *Canadian Journal Gastroenterology* 1990;4:46
31. Andersson T, Bergstrand R, Cederberg C, et al. Omeprazole treatment does not affect the metabolism of caffeine. [Abstract] *Clinical Pharmacology & Therapeutics* 1991;49:PII-95
32. Rademaker J, W, Cederberg C, Hunt RH. Refractory peptic ulcers with normal omeprazole pharmacokinetics. [Abstract] *Gastroenterology* 1991;100:(5 Part 2)A145
33. Armstrong D, Viani F, Siegrist H, et al. Does omeprazole increase gastric bacterial counts, nitrite or total nitroso compounds NOC in healthy subjects? [Abstract] *Gastroenterology* 1992;102:(4 part 2)A34
34. Cederberg C, Thomson ABR, Kirdeikis P, et al. Effect of continuous intravenous infusion of omeprazole on 24-hour intragastric pH in fasting DU-patients. Comparison to repeated bolus doses of omeprazole or ranitidine. [Abstract] *Gastroenterology* 1992;102:(4 Part 2)A48
35. Viani F, Idstrom J, Emde C, et al. Does omeprazole cause gastric anacidity in healthy subjects? [Abstract] *Gastroenterology* 1992;102:(4 Part 2)A945
36. Armstrong D, Verdu EF, Fraser R, et al. *Helicobacter pylori* infection augments the antisecretory effect of omeprazole. [Abstract] *Acta Gastroenterol Belg* 1993;56:(Suppl)129
37. Bell N, J, Rohss K, Cederberg C, et al. Does tachyphylaxis and-or rebound acid secretion occur during- after treatment with omeprazole or ranitidine? [Abstract] *Gastroenterology* 1993;104:(4)A41
38. Idstrom J, Wrangstadh M, Bergstrand R, et al. Antibiotics in gastric juice after i.v. injection. [Abstract] *Gastroenterology* 1994;106:(4)A98

39. Verdu EF, Armstrong D, Fraser R, et al. Interaction between *Helicobacter pylori* infection and acid inhibition by omeprazole. [Abstract] *Hepatogastroenterology* 1994;41:94
40. Bercik P, Verdu EF, Armstrong D, et al. *H. pylori* related increase in omeprazole (OME) effect is associated with ammonia production. [Abstract] *Gastroenterology* 1996;110:(4)A64
41. Verdu EF, Bercik P, Armstrong D, et al. Production of volatile amines by *Helicobacter pylori* (HP) is not relevant in vivo. [Abstract] *Gastroenterology* 1996;110:(4)A285
42. Bercik P, Verdu EF, Armstrong D, et al. Apparent increase in acid output during omeprazole (OME) after cure of *H. pylori* infection (HpI). [Abstract] *Gastroenterology* 1997;112:(4)A70
43. Lind T, Megraud F, Bardhan KD, et al. The MACH2 study:Antimicrobial resistance in *Helicobacter pylori* therapy - the impact of omeprazole. [Abstract] *BMJ* 1997;A89
44. Pantoflickova D, Martinek J, Blum AL, et al. The "second strike" concept of proton pump inhibition: closely spaced omeprazole administration in *H. pylori* infection. [Abstract] *Gastroenterology* 1998;in press: